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CLAIMS

1. A composition, for delivery of a therapeutic agent to a neuronal cell,
comprising:
5 the therapeutic agent, and

a neuronal cell targeting component, which component comprises a H_c
domain of botulinum C₁ toxin, or a fragment, variant, or derivative
10 thereof, which retains the function of the native H_c domain.
2. A composition according to Claim 1 further comprising a domain for
translocation of the therapeutic agent into a cell.
- 15 3. A composition according to Claim 2 wherein the translocation domain
is derived from a clostridial source.
4. A composition according to Claim 2 wherein the translocation domain
is derived from a non-clostridial source.
- 20 5. A composition according to Claim 3 wherein the translocation domain
is derived from *C. botulinum*, *C. butylicum*, *C. argentinense* or *C.
tetani*.
- 25 6. A composition according to Claim 4 wherein the translocation domain
is derived from diphtheria toxin, *Pseudomonas* exotoxin A, influenza
virus haemagglutinin fusogenic peptides or amphiphilic peptides.
- 30 7. A composition according to Claim 2, wherein the translocation domain
is derived from botulinum C₁ toxin and fragments, variants and
derivatives thereof, or diphtheria toxin and fragments, variants and
derivatives thereof.
- 35 8. A composition according to Claim 2 wherein the translocation domain
is a membrane disrupting peptide.
9. A composition according Claim 1, wherein the therapeutic agent is

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selected from the group consisting of drugs, growth factors, enzymes, DNA, modified viruses, drug release systems, or a combination thereof.

- 5 10. A composition according to Claim 9, wherein the therapeutic agent inhibits at least one member of the Rho family of GTPases.
11. A composition according to Claim 10, wherein the therapeutic agent is a C3 enzyme.
- 10 12. A composition according to Claim 11, wherein the C3 enzyme is derived from *C. botulinum*, *C. limosum*, *B. cereus*, *S. aureus*, *C. acetobutylicum*, *S. pyogenes*, *L. monocytogenes*.
- 15 13. A composition according to Claim 11 wherein the C3 enzyme is selected from the group consisting of C3Stau2, C3Stau1, and C3bot.
14. A composition according to Claim 11 wherein the C3 enzyme is selected from SEQ ID Nos: 1-10.
- 20 15. A composition according to any preceding claim wherein the H_c domain is made recombinantly.
- 25 16. A composition according any preceding claim, wherein the therapeutic agent and the H_c domain are joined to each other directly or via a linker molecule.
- 30 17. A composition according to any of Claims 2-15 wherein the therapeutic agent, the H_c domain and the translocation domain are joined to each other directly or via a linker molecule.
- 35 18. A composition according to Claim 16 or 17, wherein the linker molecule is selected from the group consisting of (GGGGS)₂, (GGGGS)₃, the interdomain linker of cellulase, PPPIEGR, collagen-like spacer, trypsin-sensitive diphtheria toxin peptide, or SEQ ID Nos: 16-24.
19. A composition according to any preceding claim wherein the

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composition is a single polypeptide.

20. A composition according to any of Claims 1-18 , wherein the composition is a dichain polypeptide.

21. A composition according to any preceding claim, wherein the composition is a suspension, emulsion, solution or a freeze-dried powder.

22. A composition according to any preceding claim, wherein the construct of the invention is re-suspended or diluted in a pharmaceutically acceptable liquid.

23. A method of making a composition of the invention according to any of Claims 1-22 comprising expressing a DNA encoding the therapeutic agent and the neuronal cell targeting domain.

24. Use of the composition of any of Claims 1-22 for the manufacture of a medicament for promoting nerve regeneration.

25. A polypeptide construct comprising an inhibitor of a member of the Rho family of GTPases, for use in neuronal cell therapy.

26. A polypeptide according to Claim 25 further comprising a neuronal cell targeting component, which component comprises a H_c domain of botulinum C₁ toxin, or a fragment, variant, or derivative thereof, which retains the function of the native H_c domain,

and a domain for translocation of the therapeutic agent into a cell.

27. A polypeptide according to Claim 26 wherein the translocation domain is derived from a clostridial source.

28. A polypeptide according to Claim 26 wherein the translocation domain is derived from a non-clostridial source.

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29. A polypeptide according to Claim 27 wherein the translocation domain is derived from *C. botulinum*, *C. butylicum*, *C. argentinense* or *C. tetani*.
- 5 30. A polypeptide according to Claim 28 wherein the translocation domain is derived from diphtheria toxin, *Pseudomonas* exotoxin A, influenza virus haemagglutinin fusogenic peptides or amphiphilic peptides.
- 10 31. A polypeptide according to Claim 26, wherein the translocation domain is derived from botulinum C₁ toxin and fragments, variants and derivatives thereof, or diphtheria toxin and fragments, variants and derivatives thereof.
- 15 32. A polypeptide according to Claim 26 wherein the translocation domain is a membrane disrupting peptide.
33. A polypeptide according to Claim 25, wherein the inhibitor is a C3 enzyme.
- 20 34. A polypeptide according to Claim 33, wherein the C3 enzyme is derived from *C. botulinum*, *C. limosum*, *B. cereus*, *S. aureus*, *C. acetobutylicum*, *S. pyogenes*, *L. monocytogenes*.
- 25 35. A polypeptide according to Claim 33 wherein the C3 enzyme is selected from the group consisting of C3Stau2, C3Stau1, and C3bot.
36. A polypeptide according to Claim 33 wherein the C3 enzyme is selected from SEQ ID Nos: 1-10.
- 30 37. A polypeptide according to any of Claims 25-36 wherein the H_c domain is made recombinantly.
38. A polypeptide according any of Claims 25-37, wherein the inhibitor and the H_c domain are joined to each other directly or via a linker molecule.

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39. A polypeptide according to any of Claims 26-37 wherein the inhibitor, the Hc domain and the translocation domain are joined to each other directly or via a linker molecule.
- 5 40. A polypeptide according to Claim 38 or 39, wherein the linker molecule is selected from the group consisting of (GGGGS)₂, (GGGGS)₃, the interdomain linker or cellulase, PPPIEGR, collagen-like spacer, trypsin-sensitive diphtheria toxin peptide, or SEQ ID Nos: 16-24.
- 10 41. A polypeptide according to any of Claims 25-40, wherein the polypeptide is a single chain.
42. A polypeptide according to any of Claims 25-40, wherein the polypeptide is a dichain.
- 15 43. A polypeptide according to any of Claims 25-42, wherein the polypeptide is re-suspended or diluted in a pharmaceutically acceptable liquid.
- 20 44. A polypeptide according to any of Claims 25-42, wherein the polypeptide is contained in a suspension, solution, emulsion, or a freeze-dried powder.
- 25 45. Use of a polypeptide of any of Claims 25-44, for the manufacture of a medicament for neuronal cell therapy.
46. Use of an inhibitor of a member of the Rho family of GTPases, for use in the manufacture of a medicament for neuronal cell therapy.
- 30 47. Use according to Claim 46 of a C3 enzyme.
48. Use according to Claim 47 wherein the C3 enzyme is derived from *C. botulinum*, *C. limosum*, *B. cereus*, *S. aureus*, *C. acetobutylicum*, *S. pyogenes*, *L. monocytogenes*.
- 35 49. Use according to Claim 47 wherein the C3 enzyme is selected from the group consisting of C3Stau2, C3Stau1, and C3bot.

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50. Use according to Claim 47 wherein the C3 enzyme is selected from SEQ ID Nos: 1-10.